

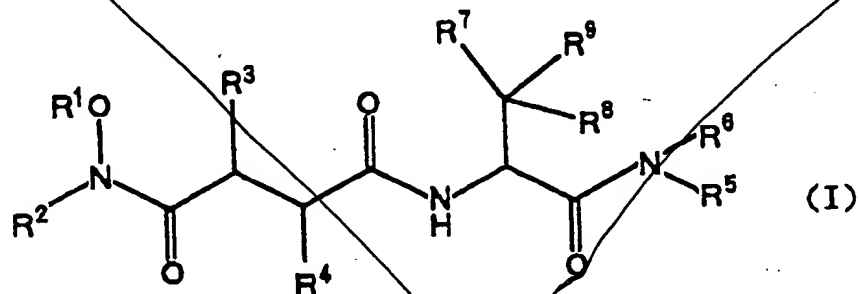


In the Claims:

Kindly cancel claim 1 without prejudice.

Please amend the claims as follows:

2. (Amended) A compound having the following formula (I):



wherein

R¹ and R² are hydrogen;
R³ is selected from the group consisting of (C₁-C₉) alkyl, (C₃-C₇) cycloalkyl-substituted lower (C₁-C₄) alkyl, amino-substituted (C₁-C₆) alkyl, phenyl-lower (C₁-C₄) alkyl, guanido-substituted phenyl-lower (C₁-C₄) alkyl, amino-substituted phenyl-lower (C₁-C₄) alkyl, carboxy-substituted phenyl-lower (C₁-C₄) alkyl, carbamoyl-substituted phenyl-lower (C₁-C₄) alkyl, hydroxy-substituted phenyl-lower (C₁-C₄) alkyl, guanido-substituted lower (C₁-C₄) alkyl-substituted phenyl-lower (C₁-C₄) alkyl, unprotected or optionally protected

amino-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, hydroxy-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, lower (C_1-C_4) alkoxy-carbonyl-substituted phenyl-lower (C_1-C_4) alkyl, lower (C_1-C_4) alkylimino-substituted (C_1-C_6) alkyl, lower (C_1-C_4) acylimido-alkyl-substituted (C_1-C_6) alkyl, arylmethylimino-substituted (C_1-C_6) alkyl, nitrogen-containing heterocyclic radical-substituted lower (C_1-C_4) alkylimino-substituted (C_1-C_6) alkyl, nitrogen-containing heterocyclic radical-substituted lower (C_1-C_4) alkyl, oxygen-containing (C_1-C_8) straight chain or branched alkyl, arylsulfonamido-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, alkylsulfonamido-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, aryloxy-substituted lower (C_1-C_4) alkyl, and hydroxy-substituted (C_1-C_8) alkyl;

R^4 is selected from the group consisting of (C_3-C_9) alkyl, hydroxy-substituted (C_3-C_8) alkyl, and unsubstituted or optionally substituted aryl-lower (C_1-C_4) alkyl;

R^5 is selected from the group consisting of lower (C_1-C_4) alkyl, (C_3-C_7) cycloalkyl, mono- or di-lower (C_1-C_4) alkylamino-substituted lower (C_1-C_4) alkyl, carboxy-substituted lower (C_1-C_4) alkyl, hydroxy-substituted (C_1-C_6) alkyl, bis(phosphono)-hydroxymethyl-substituted (C_1-C_{11}) alkyl, tetrabenzyl bis(phosphono)hydroxymethyl-substituted (C_1-C_{11}) alkyl, and a nitrogen-containing heterocyclic radical;

R^6 is hydrogen;

R^7 is hydrogen or lower (C_1-C_4) alkyl;

R^8 is hydrogen or lower (C_1-C_4) alkyl; and

R^9 is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula: $-X-Y$

wherein X is (C_1-C_6) alkylene or phenylene, and

Y is a group of the formula: $-A-B$ or $-B$

wherein B is selected from the group consisting of hydrogen, amino, amidino, lower (C_1-C_4) acylimido, unsubstituted or

optionally substituted benzimidoyl, bis(phosphono)methyl, tetra-lower (C_1-C_4) alkyl bis(phosphono)methyl, tri-lower (C_1-C_4) alkyl bis(phosphono)methyl, bis(phosphono)hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and lower (C_1-C_4) alkyl-substituted imidazol-3-yl, and
A is selected from the group consisting of lower (C_1-C_4) alkylene, imino, and lower (C_1-C_4) alkylene-imino;
provided that a combination wherein R^7 is methyl, R^8 is methyl and R^9 is methyl is excluded;
or a pharmaceutically acceptable salt or solvate thereof.

d. (Amended) The compound according to claim 2, wherein

R^1 and R^2 are hydrogen;

R^3 is selected from the group consisting of methyl, isobutyl, aminopropyl, phenylpropyl, guanidophenylpropyl, aminophenylpropyl, hydroxyphenylpropyl, carboxyphenylpropyl, carbamoylphenylpropyl, aminomethylphenylpropyl, guanidomethylphenylpropyl, hydroxymethylphenylpropyl, aminomethylbenzyl, toluenesulfonamidomethylbenzyl, methanesulfonamidomethylbenzyl, isobutyliminomethylbenzyl, phthalimidomethylbenzyl, phenoxyethyl, aminopentyl, acetimidoyliminopentyl, isobutyliminopentyl, pyridylmethyliminopentyl, methoxycarbonylphenylpropyl, ethoxyethoxyethyl, hydroxyoctyl, butoxyethyl, isobutyloxyethyl, morpholinopropyl, (3,4,4-trimethyl-2,5-dioxo-imidazolidin-1-yl)propyl, cyclohexylpropyl, and piperidinopropyl;

R^4 is selected from the group consisting of naphthylmethyl, phenylpropyl, isobutyl, tert-butyl, isopropyl, and hydroxyoctyl;

R^5 is selected from the group consisting of methyl, cyclopropyl, 2-(N,N-dimethylamino)ethyl, 2-carboxyethyl, 2-hydroxyethyl, 2-hydroxy-1,1-dimethylethyl, 2-hydroxy-1-methylethyl, 6,6-bis(phosphono)-6-hydroxyhexyl, tetrabenzyl 6,6-bis(phosphono)-6-hydroxyhexyl, piperidyl, and morpholinyl;

R^6 is hydrogen;

R^7 is hydrogen or methyl;

R^8 is hydrogen or methyl; and

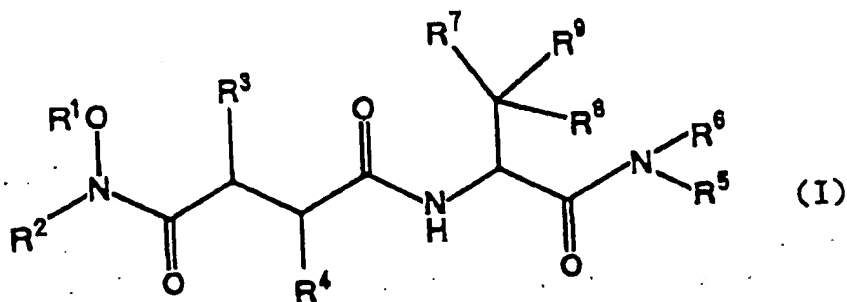
R^9 is selected from the group consisting of hydrogen, hydroxy, amino, and a group of the formula: $-X-Y$ wherein X is selected from the group consisting of methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, and phenylene, and

Y is a group of the formula: $-A-B$ or $-B$ wherein B is selected from the group consisting of amino, amidino, acetimidoyl, propionimidoyl, benzimidoyl, bis(phosphono)methyl, tetraethyl bis(phosphono)methyl, triethyl bis(phosphono)methyl, tetramethyl bis(phosphono)methyl, trimethyl bis(phosphono)methyl, bis(phosphono)hydroxymethyl, tetrabenzyl bis(phosphono)hydroxymethyl, and 2-methyl-imidazol-3-yl, and

A is selected from the group consisting of imino, methyleneimino, and methylene.

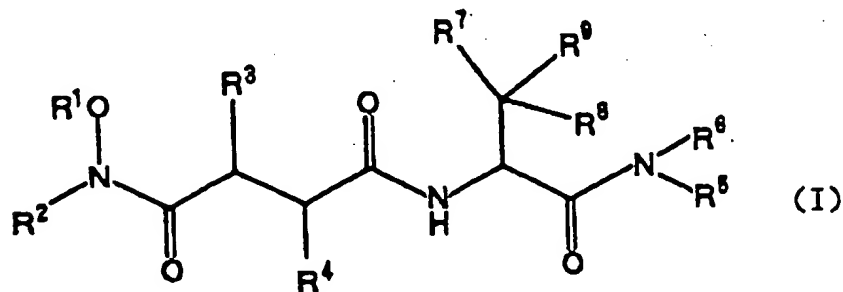
(Twice Amended)

4. ~~(Amended)~~ A pharmaceutical or veterinary composition which comprises (a) an effective amount of at least a member selected from the group consisting of a compound of the formula (I):



wherein R^1 to R^9 , all have the same meanings as defined in claim 1b, and a pharmaceutically or veterinarily acceptable salt or solvate thereof, and (b) a pharmaceutically or veterinarily acceptable excipient or carrier.

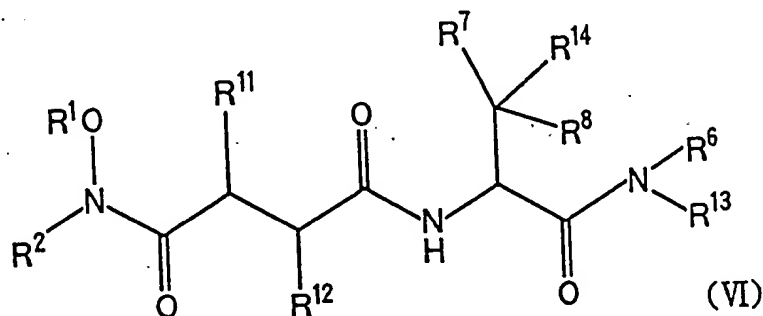
5. ^(Twice Amended)
~~(Amended)~~ A metalloproteinase inhibitor which comprises an effective amount of at least a member selected from the group consisting of a compound of the formula (I):



wherein R^1 to R^9 , all have the same meanings as defined in claim 16², and a pharmaceutically acceptable salt or solvate thereof.

8. ^(Twice Amended)
~~(Amended)~~ A method of prophylactically and/or therapeutically treating diseases and/or disorders associated with tissue degradation comprising administering an effective amount of the compound according to claim 16².

12. ^(Twice Amended)
~~(Amended)~~ A compound having the following formula (VI):



wherein R^1 , R^2 , and R^6 to R^8 , all have the same meanings as defined in claim 16².

R^{11} has the same meaning as defined for R^3 , or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted phenyl-lower (C_1-C_4) alkyl, nitro-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted (C_1-C_6) alkyl, nitro-substituted (C_1-C_6) alkyl, protected carboxy-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-substituted phenyl-lower (C_1-C_4) alkyl, protected guanido-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected carboxy-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-containing (C_1-C_8) straight chain or branched alkyl, and cyano-substituted phenyl-lower (C_1-C_4) alkyl;

R^{12} has the same meaning as defined for R^4 , or is protected hydroxy-substituted (C_1-C_8) alkyl;

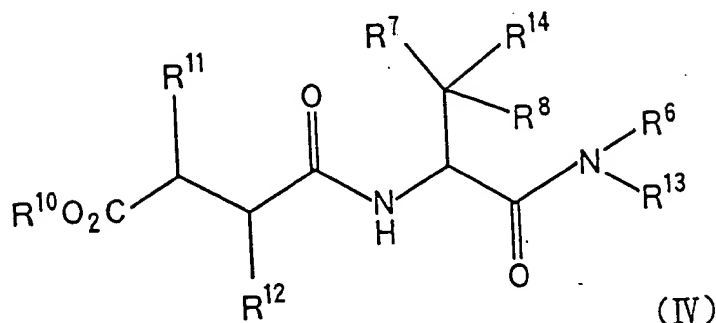
R^{13} has the same meaning as defined for R^5 , or is selected from the group consisting of protected carboxy-substituted lower (C_1-C_4) alkyl, protected hydroxy-substituted lower (C_1-C_4) alkyl, protected bis(phosphono)hydroxymethyl-substituted (C_1-C_{11}) alkyl, and a protected nitrogen-containing heterocyclic group; and

R^{14} has the same meaning as defined for R^9 , or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula: $-X-E$ or $-X-A-E$

wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, (C_1-C_{11}) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimido, protected benzimidoyl, protected bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl, and protected (C_1-C_{11}) alkyl-substituted imidazol-3-yl;

or a salt thereof.

13. ^(Twice Amended)
~~(Amended)~~ A compound having the following formula (IV):



wherein R^6 to R^8 , all have the same meanings as defined in claim

162.
 R^{10} is selected from the group consisting of unsubstituted or optionally substituted alkyl, unsubstituted or optionally substituted aralkyl, and a carboxy-protecting group;

R^{11} has the same meaning as defined for R^3 , or is selected from the group consisting of protected hydroxy, protected guanido-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted phenyl-lower (C_1-C_4) alkyl, nitro-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted (C_1-C_6) alkyl, nitro-substituted (C_1-C_6) alkyl, protected carboxy-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-substituted phenyl-lower (C_1-C_4) alkyl, protected guanido-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected amino-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected carboxy-substituted lower (C_1-C_4) alkyl-substituted phenyl-lower (C_1-C_4) alkyl, protected hydroxy-containing (C_1-C_8) straight chain or branched alkyl, and cyano-substituted phenyl-lower (C_1-C_4) alkyl;

R^{12} has the same meaning as defined for R^4 , or is protected hydroxy-substituted (C_1-C_8) alkyl;

bis(phosphono)methyl, protected bis(phosphono)hydroxymethyl,
and protected (C₁-C₁₁) alkyl-substituted imidazol-3-yl;

R¹³ has the same meaning as defined for R⁵, or is selected from the group consisting of protected carboxy-substituted lower (C₁-C₄) alkyl, protected hydroxy-substituted lower (C₁-C₄) alkyl, protected bis(phosphono)hydroxymethyl-substituted (C₁-C₁₁) alkyl, and a protected nitrogen-containing heterocyclic group; and

R¹⁴ has the same meaning as defined for R⁹, or is selected from the group consisting of protected amino, protected hydroxy, and a group of the formula: -X-E or -X-A-E

wherein X and A, both have the same meanings as given above, and E is selected from the group consisting of nitro, cyano, amino, carboxyl, (C₁-C₁₁) hydroxyalkyl, protected amino, protected guanido, protected amidino, protected acylimido, protected benzimidoyl, protected

or a salt thereof.